Fabric Apprat, et al
Famil Mammalian Potassium Channels, Their Chan
And Their Use, Especially for The Screening of Drugs

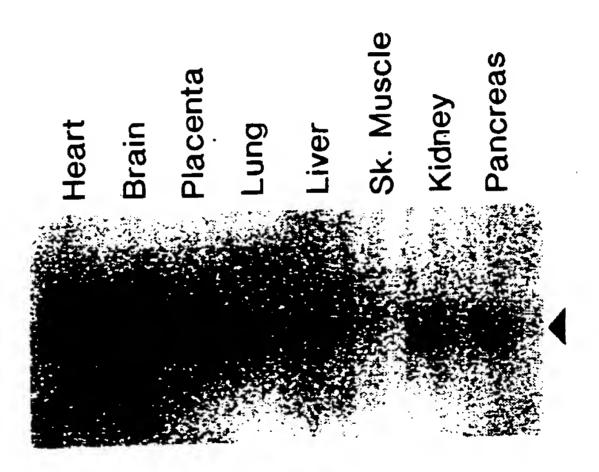


FIG. 1A

## 1201-CIP-DIV-2-00 Febrice Duprat, et al hily of Mammalian Potassium Channels, Cloning Thid Their Use, Especially for The Screening of Drugs

gggg aaga	cggg	cggg	cgcg	cggg cact	ggag ccgg	cggg	cggc	gggc	ggga gttg	gcca	ggcc	cggg	cggg	ggcg	cgct gggg ggcg	cggc	gggg	ccag	-153 -77 -1
															CGG R		_		57 19
GCC	TGG	TGC	TTC	GGC	TTC	CTG	GTG	CTG	GGC	TAC	TTG	CTC	TAC	CTG	GTC	TTC	GGC	GCA	114
A	W	C	F	G	F	L	V	L	G	Y	L	L	Y	L	V	F	G	A	38
GTG	GTC	TTC	TCC	TCG	GTG	GAG	CTG	CCC	TAT	GAG	GAC	CTG	CTG	CGC	CAG	GAG	CTG	CGC	171
V	V	F	S	S	V	E	L	P	Y	E	D	L	L	R	Q	E	L	R	57
AAG	CTG	aag	CGA	CGC	TTC	TTG	GAG	GAG	CAC	GAG	TGC	CTG	TCT	GAG	CAG	CAG	CTG	GAG	228
K	L	K	R	R	F	L	E	E	H	E	C	L	S	E	Q	Q	L	E	76
CAG	TTC	CTG	GGC	CGG	GTG	CTG	GAG	GCC	AGC	AAC	TAC	GGC	GTG	TCG	GTG	CTC	AGC	AAC	285
Q	F	L	G	R	V	L	E	A	S	N	Y	G	V	S	V	L	S	N	95
GCC	TCG	GGC	AAC	TGG	AAC	TGG	GAC	TTC	ACC	TCC	GCG	CTC	TTC	TTC	GCC	AGC	ACC	GTG	342
A	S	G	N	W	N	W	D	F	T	S	A	L	F	F	A	S	T	V	114
CTC	TCC	ACC	ACA	GGT	TAT	GGC	CAC	ACC	GTG	CCC	TTG	TCA	GAT	GGA	GGT	AAG	GCC	TTC	399
L	S	T	T	G	Y	G	H	T	V	P	L	S	D	G	G	K	A	F	133
TGC	ATC	ATC	TAC	TCC	GTC	ATT	GGC	ATT	CCC	TTC	ACC	CTC	CTG	TTC	CTG	ACG	GCT	GTG	456
C	I	I	Y	S	V	I	G	I	P	F	T	L	L	· F	L	T	A	V	152
GTC V	CAG Q	CGC R	ATC	ACC T	GTG V	CAC H	GTC V	ACC T	CGC R	AGG R	CCG	GTC V	CTC L	TAC Y	TTC F	CAC H	ATC I	CGC R	513 171
TGG	GGC	TTC	TCC	: AAG	CAG	GTG	GTG	GCC	ATC	GTC	CAT	GCC	GTG	CTC	CTT	GGG	TTT	GTC	570
W	G	F	S	K	Q	V	V	A	I	V	H	A	V	L	L	G	F	V	190
ACT	GTO	TCC	TGC	TTC	TTC	TTC	ATC	CCG	GCC	GCT	GTC	TTC	TCA	GTC	CTG	GAG	GAT	GAC	627
T	V	S	C	F	F	F	I	P	A	A	V	F	S	V	L	E	D	D	209

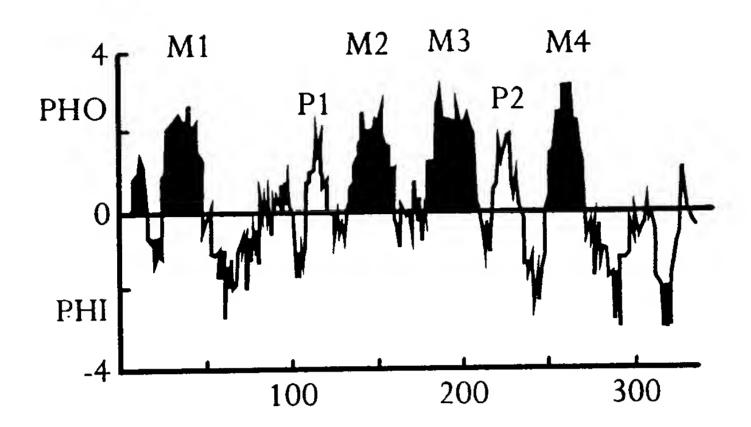
FIG. 1B-1

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And Their Use, Especially for The Screening of Drugs

TGG	AAC	TTC	CTG	GAA	TCC	TTT	TAT	TTT	TGT	TTT	ATT	TCC	CTG	AGC	ACC	ATT	GGC	CTG	68
W	N	F	L	E	S	F	Y	F	C	F	I	S	L	S	T	I	G	L	22
GGG	GAT	TAT	GTG	CCT	GGG	GAA	GGC	TAC	AAT	CAA	AAA	TTC	AGA	GAG	CTC	TAT	aag	ATT	74
G	D	Y	V	P.	G	E	G	Y	N	Q	K	F	R	E	L	Y	K	I	24
GGG	ATC	ACG	TGT	TAC	CTG	CTA	CTT	GGC	CTT	ATT	GCC	ATG	TTG	GTA	GTT	CTG	GAA	ACC	79
G	I	T	C	Y	L	L	L	G	L	I	A	M	L	V	V	L	E	T	26
TTC	TGT	GAA	CTC	CAT	GAG	CTG	AAA	AAA	TTC	AGA	AAA	ATG	TTC	TAT	GTG	AAG	AAG	GAC	85
F	C	E	L	H	E	L	K	K	F	R	K	M	F	Y	V	K	K	D	28
AAG	GAC	GAG	GAT	CAG	GTG	CAC	ATC	ATA	GAG	CAT	GAC	CAA	CTG	TCC	TTC	TCC	TCG	ATC	9:
K	D	E	D		V	H	I	I	E	H	D	Q	L	S	F	S	S	I	3(
ACA	GAC	CAG	GCA	GCT	GGC	ATG	AAA	GAG	GAC	CAG	AAG	CAA	AAT	GAG	CCT	TTT	GTG	GCC	9
T	D	Q	A		G	M	K	E	D	Q	K	Q	N	E	P	F	V	A	3
tta aag tct gga aaa gag	Q ctag tgtc cgac aact igcat	actt gacc ctta ttgg agag	taag cata ggtt atgt tcaa	A ggtc aaat cagg ggag tgca gttt actc	C aggg agct atgt gaga ttta acta	actg ctaa atac gatc aata ttta	D agga tttg tatg attt ggtt taat .ccag	G agag caat tgag agca agct tatg gcat	P gctt gtct gaaa gtat gatg tgta aggt	A aagt tatt tgag gcta gcta aacc	aaaa atgt ctgt aata tttg atta ttct	H tcat aaca ccac ggtt gcaa gcatg acta	tttt acaa ctaa agaa aatt stacc itgta	atca aaaa aatt gcag tata caco	gaat agad cata tata taaa	gcaa acat tgtg tata gaag atga gtat	aago ggaa acaa cttt caaa ttat aaat	gcatt gaaaa caaag aatta taact aaaaa ttttg atgtt gtttct	10 3 11 11 12 13 14 14 15 16 17

FIG. 1B-2

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And Their Use, Especially for The Screening of Trugs



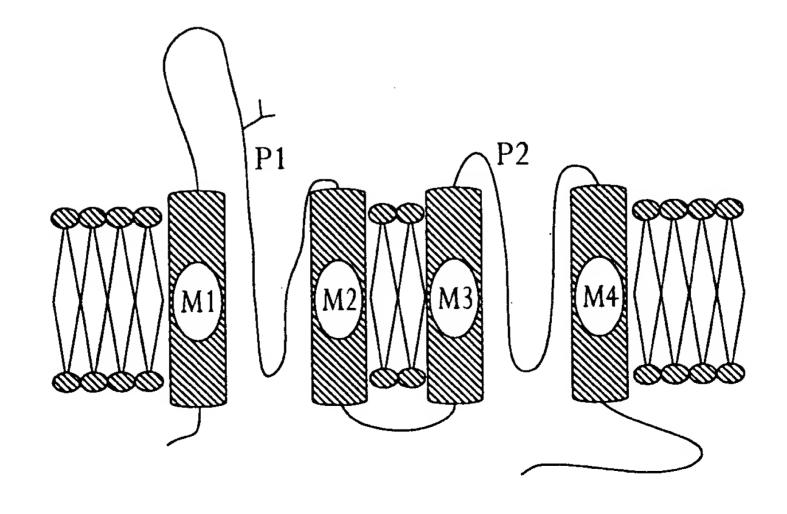


FIG. 1C

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And Their Use, Especially for The Screening of Drugs

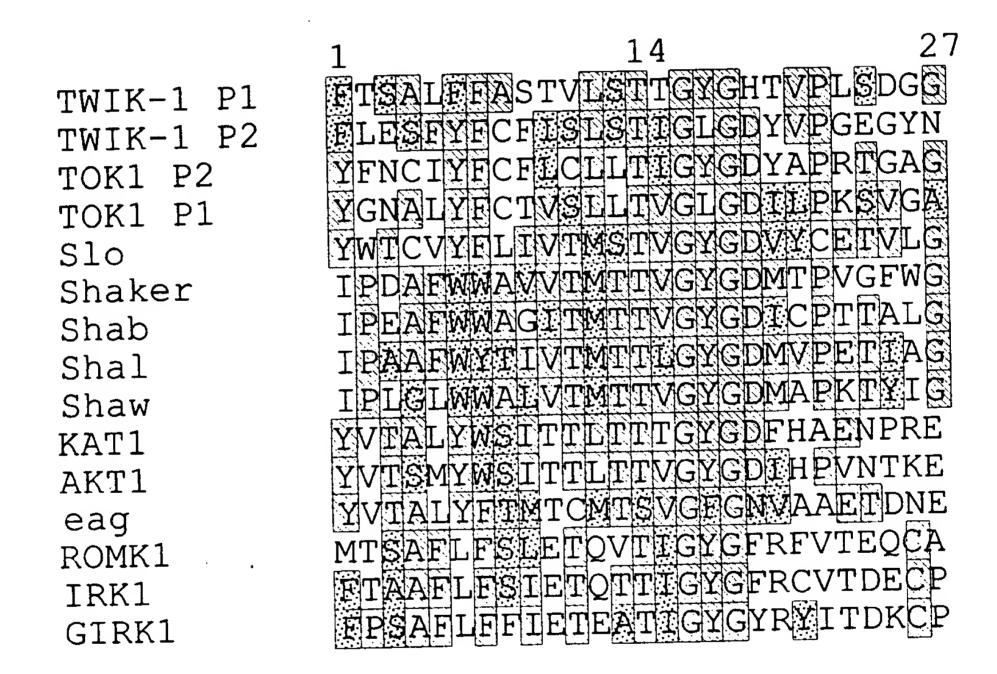


FIG. 2A

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And Their Use, Especially for The Screening of Drugs

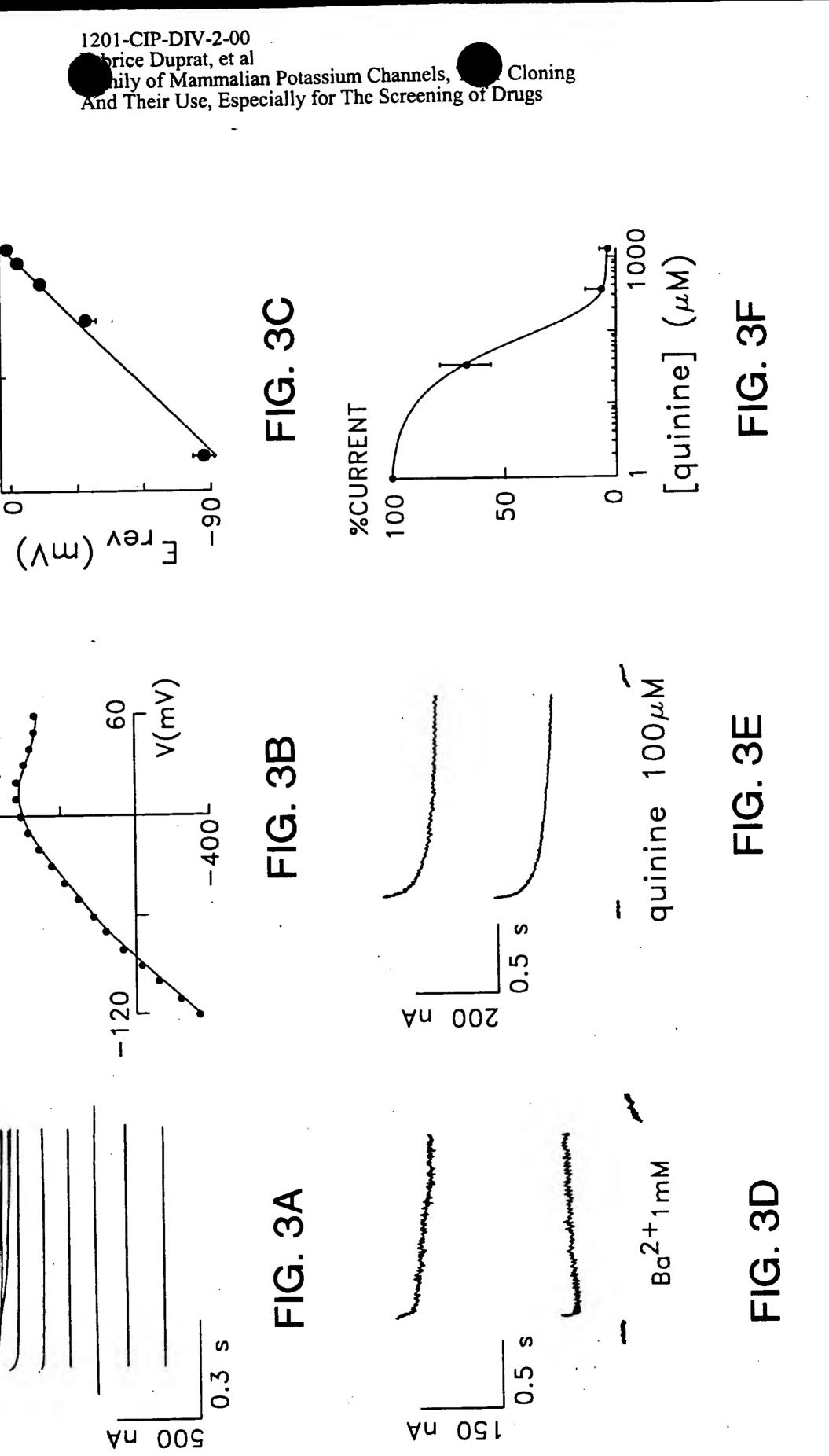
TWIK-1 f17c8 M110-2	1 1	MLQSLAGSSCVREVERHRSAWCFGELVVGY MYTDEGEYSGDTDHGGSTMQKMSPNTRONFRQNVNVVVCLSAAITI MYTDEGEYSGDTDHGGSTMQKMSPNTRONFRQNVNVVVCLSAAITI MTVSMEENSKIDMLSATSKDKKVATDRSLLNKVHLGPLALHTGLVLSC
TWIK-1 f17c8 M110-2	31 47 49	LEYLVEGAVVESSVELEVEDELROEDLRKEKRRETEEHECL  LVENLIGAGIEDVLAETOWSSES  VTVALGGAVET STEHEDEEEKRREKAIREFODEKOOFWGNITSGIEN
TWIK-1 f17c8 M110-2	71 69 96	SEODLEDELGRYLEASNYGVSVLSNASGNWNW-DETSALT LNEWSEVSKCLHNLPIGGKITAEMKSKLGKCLTKSSRIDGFGKAIT SEOSLELYTKKLILMLEDAHNAHAELYFFLNHEIPKDMW-TESSALV
TWIK-1 f17c8 M110-2	110 115 142	FASTVESTIGEGHTVPLSDGGKAFCII-VSVLGIPFTLLFTTAVVORI FSWTLYSTVGYGSLYPHSTLGRYLTIF-YSLLMIPVFIAFKFEFGTFI FTTTVIPVGYGYLTPVSAYGR-WCLIAYALLGIPLTLYTMADIGKEA
TWIK-1 f17c8 M110-2	157 162 189	TVHVERRPULVEHERWGESKOVVALVHAVLLGEVIVSCIF AHFLVVVSNRTRLAVKKAVYKLS-ONPENAETPSNSLOHDYLIFLSSL AQLVTR
TWIK-1 f17c8 M110-2	197 209 213	FIL-PARVESVLEDDWNELESFYFCFISESTIGLEDYVRGEGYN LUCSESTLESSALESSIENTSYLSSVYFGITTMFLIGTEDIVPTN FAYPLVVGFILCSTSNITYLDSVYFSLTSIETIGFEDLTP
TWIK-1 f17c8 M110-2	239 254 253	OKFRETYKTGETCYLELGLIAMLVVLETFCELHELKKER
TWIK-1 f17c8 M110-2	278 295 294	
TWIK-1 f17c8 M110-2	315 338 342	EKLISSIPST CIVERREDESAENSARNIFIS

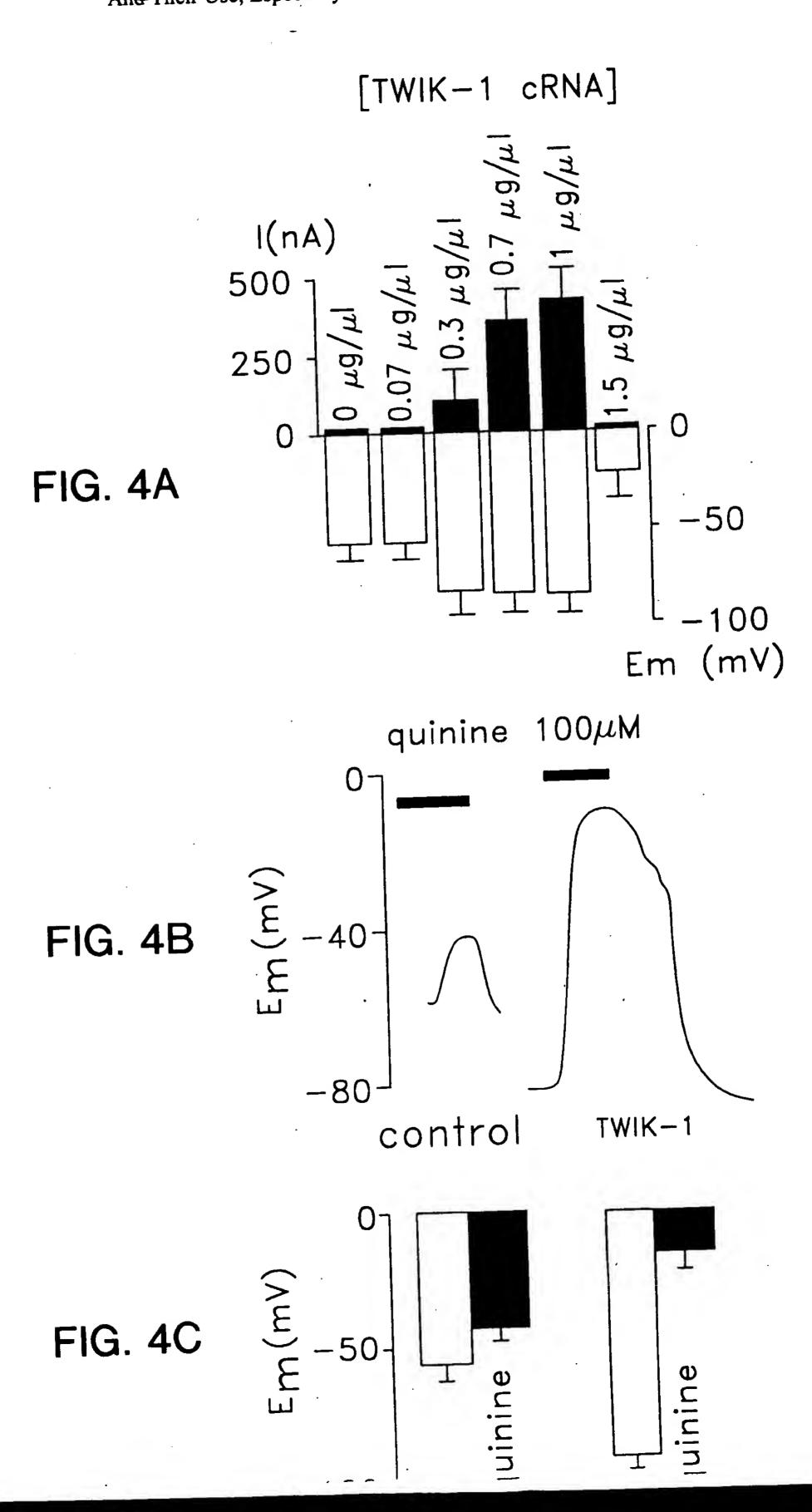
FIG. 2B

100

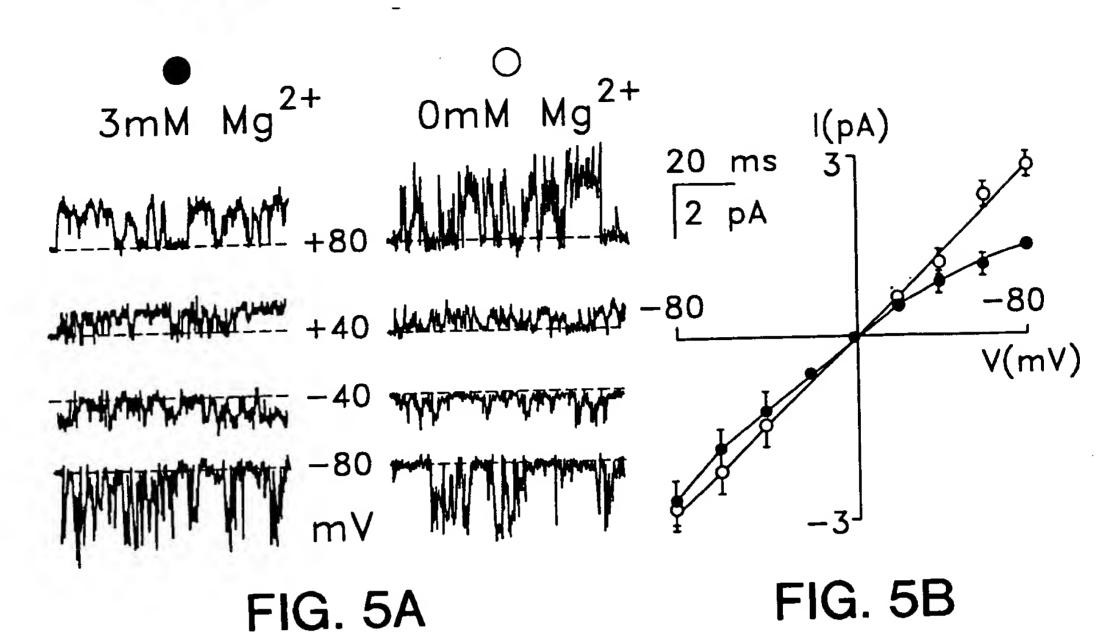
[K+] (mM) 10

800 [ I(nA)

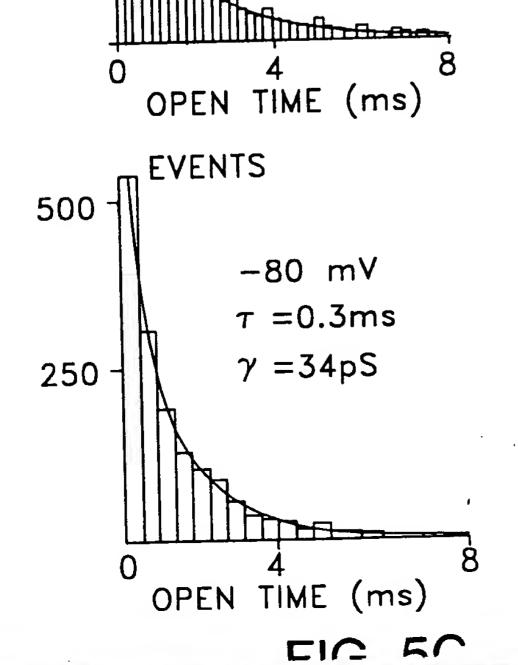


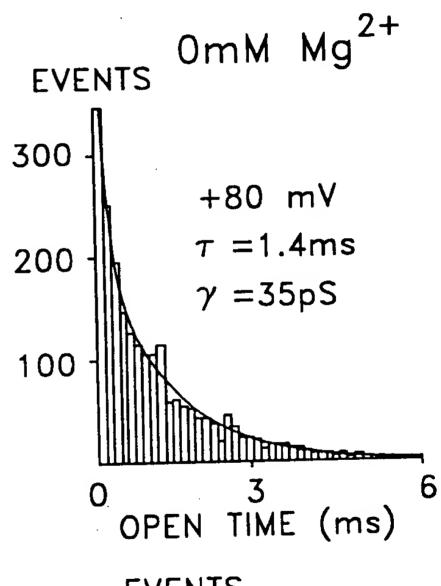


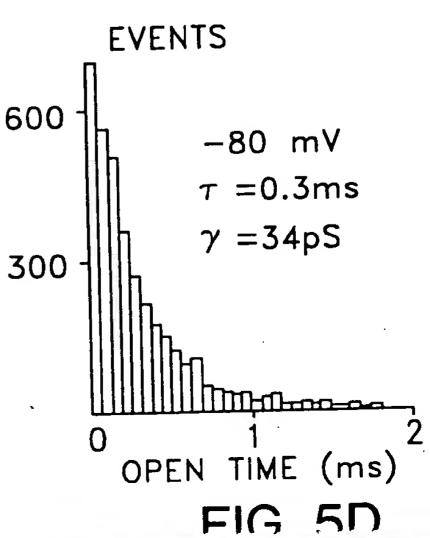
100



 $300 \begin{array}{c} 3 \text{mM Mg}^{2+} \\ \hline 300 \\ \hline \\ \tau = 1.9 \text{ms} \\ \hline \\ 200 \\ \hline \end{array}$ 









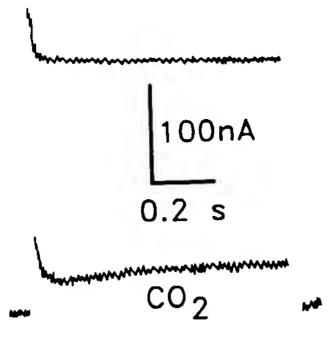


FIG. 6A

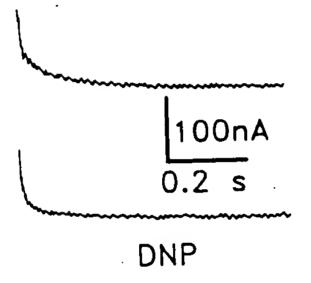


FIG. 6C

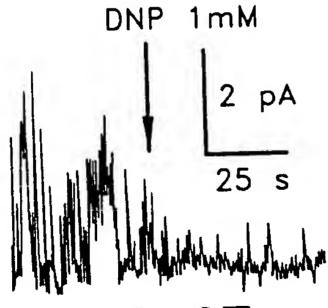


FIG. 6E

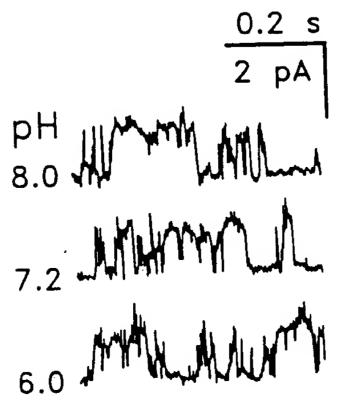


FIG. 6G

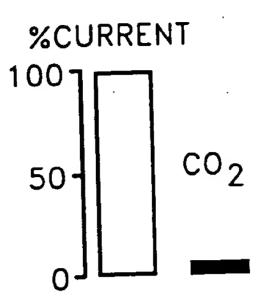


FIG. 6B

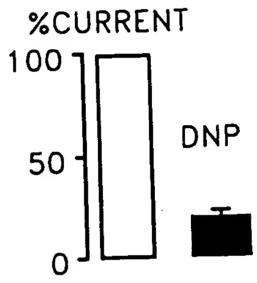


FIG. 6D

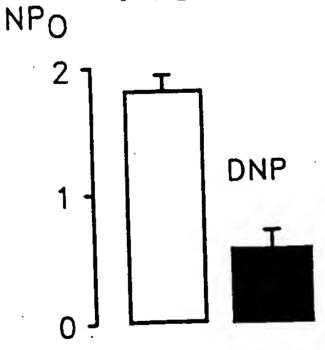


FIG. 6F

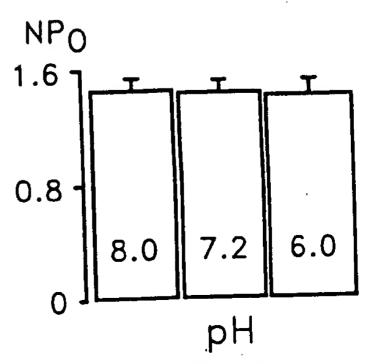


FIG. 6H

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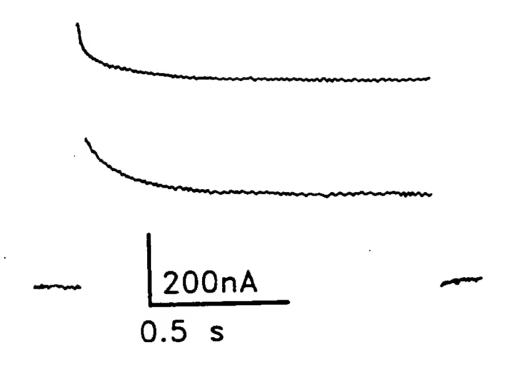


FIG. 7A

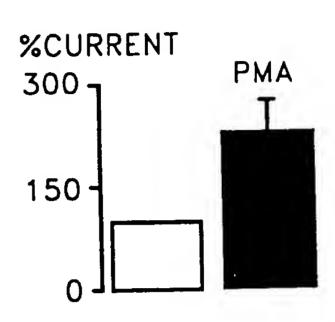


FIG. 7B

 $NP_0$ 

6

3

PMA

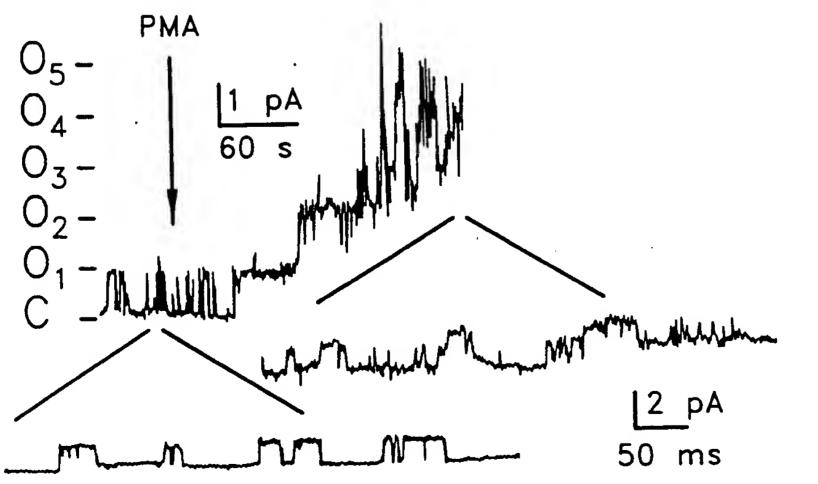


FIG. 7D

FIG. 7C

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And Their Use, Especially for The Screening of Drugs

tgccctgcgcggatagcggcgagcgcatgccccaggccgcctccg 57 CTG TAC ACC TTC TGC ACC ATC GTG CTG GCG CTC ACG CGC GTG CAG AAC CGG ATG AAG 19 L Y F C I V L L A V R N Q R M K Y F C Ι V L T L Α R V E N 114 GAG CGG ATC CTG TCG GAG CCC GAG CTG GAG **GAC** TTC **GCG GCG** GTC GGC GCC CTG GTG 38 R E I E P E S Ē L F D A V Α A G L V E R I E E M P E S L D A F V A V G A 171 GGC CAG AGC CTC CGG CGC TAC AAC GCG CTG CAG CAG GAG **CGG** CTG CTG GAG CGG CAG 57 G S Q Y L R N R A E L Q R Q E R Q E G S R Y N R A E L R Q L E L Q R 228 GGC GTG GCC CCG CAC AAG AAG CTC GTC GTG CTG CGC CGC CTG GAG GAG GAG TAC GGC 76 V G K Α P H K L R E R V V L E Y E G G V H K A K P R V L R V E Ê L Ē Y G 285 ATC GGC ATC ACC ACC GTC ACC ATC TTC GCC TAC TTC TCC GCC GGC TTC CAG CGC TGG 95 G I T V I I F A F S G F A R W Q I G Т I V T I F A F Y S A G F R W 0 342 ATG TTC TAC GCG TGC GGC TTC AAG GTG GAT GGC AGC **ACG GCA** CCC GCG GGG CAC TAC 114 Α Y F C M V F G K G D S T P Α Н A G Y F Y A C M F G G K V D S T P A Н G A Y 399 CGC ATC GGC GAG CAG AGC CTG TTC GTC ATG **ACG** CTC CTC ATC CCG CTG 133 I N G E R S L F Q V M L P G I I N E R G S F Q I L L M Ι P G L L 456 GCC CGC CGG CTG GGC ATG AAG GGG GCC AAG CAC CGC CTG CTG GTG AGG TAC 152 R R A G M G L K K R H A Y R V R K R A H GTG TCC. ATG GCC AAC ATG GTG CTC ATC GGC TTC TTC TCG TGC ATC AGC ACG CTG 513 171 C F F G V D S C Ι S V F I G V M N M Α S V GCC GCC TTC TCC CAC TAC GAG CAC TGG ACC TTC TTC CAG GCC 570 TGC ATC GGC GCC 190 F Q Α F W E H Y S H F Y F Q E R Y Y F S I G Α TAC GTG GCG CTG TAC TAC TGC TTC ATC ACC CTC ACC ACC ATC GGC TTC GGC GAC 627 209 Q D G G F I Y C Q D Y V Α F G I G T T L I F C CAG ACG CAG CCG CAG TAC GTG GCC TTC AGC TTC GTC TAC ATC 684 AAG GAC CAG GCC CTG 228 I V F S F Y Α V Q Q Q I V S F V Y Q P Q Α K D 0 GTC ATC GGC GCC TTC CTC AAC CTC GTG GTG CTG CGC 741 TTC ATG ACG 247 V N G Α M V V N L L I A F V G L L

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798 CGC ACG CTC CTG GCG CGC CAC GCC GAG AAG CGC GAC GAG GAC GAG GCC ATG AAC 266 R T L A Н R E D Α R K E D E Α N M H L R A E H A D R E K D E A N T M 855 ACC GAC ACG ACT GCG CAC AGC **GGC** GGT GGG GGA GGC GGC GGC **GCG** CAG 285 GGG AAC Ţ Α D T H \$ Α G G G G G G G Α Q G N  $\mathbf{D}$  $\mathbf{G}$ <u>s</u> L G <u>s</u> <u>S</u> 2 G G G V A Q G N 912 CTG GAG GTG TAC GCG GTC GGC GGC GGC CGC AAC TTC **GCA** GCG TCA TCC ACG GCG 304 L V E A V Y N F R G G G G A A Α S L E V Y V G GYGYGYGGS G R N F A Α ΤC **VRPRDPV** ŊΑ 969 TAC CTG AAG GAG CGC **AGC** TAC AAG TGG TGC CTG TCG TGC TCC ATG CAC TTC CAG 323 Y Q L K E S R K Y W C L S C M S F Q H Y Q K L E R S K Y L W C S C S F 0 H 1026 CAG GAG GAC ACG GTG TGC TCC TCC ACG CTC GAC CCG CGG ATC ATG ATC CCC 342 Q E V C T S D S L D R P I P M I S E H V C T D S S L D R I P I M I P S 1083 TGC CGC CGA ACG CCC TCG GAC TAC AGC GGC CGC GGC **GGG GGA** CCG TCG TCG CAC AGC 361 C S R R P D T S Y R G G G P G S S S H C S P H P D S R Y G G G P G S S H S 1140 CTG CAC AGC GGT TCC ACG GTG TCG ATC AGC GCC TCC CCA CGC GCG GGG TGC AGC CTG 380 S H G L Ţ S S S ٧ I R S A P G Α C L S H G S T V S I S A S R T Q G S C L ctgccccgagggacc 1200 AGG AGC TCC TGA GTG AAG CGC ATG CTC GGC CGC 395 V S S R R K. M G F R \$ L S S V tggagcacctggggggcgcggggggacccctgctgggaggccaggagactgcccttgctgccttctgcccagtg 1276 ggaccccgcacaacatccctcaccactctcccccagcacccccatctccgactgtgcctgcttgcaccagccggca 1352 ggaggccgggctctgaggacccctggggcccccatcggagccctgcaaattccgagaaatgtgaaacttggtgggg 1428 tcagggaggaaaggcagaagctgggagcctccctttccctttgaaaatctaagaagctcccagtcctcagagaccct 1504 gctggtaccacaccccaccttcggaggggacttcatgttccgtgtacgtttgcatctctatttatacctctgtcct 1580 gctaggtctcccaccttcccttggttccaaaagccagggtgtctatgtccaagtcacccctactcagccccactcc 1656 ccttcctcatccccagctgtgtctcccaacctcccttcgtgttgttttgcatggctttgcagttatggagaaagtg 1732 gcgagctgggaggcaggaggcagcggcctgtcagtctgcagaatggtcgcactggaggttcaagctaactggcctc 1884 cagccacattctcatagcaggtaggacttcagccttccagacactgcccttagaatctggaacagaagacttcaga 1960 ctcaccataattgctgataattacccactcttaaatttgtcgagtgatttttagcctctgaaaactctatgctggc 2036 cactgattcctttgagtctcacaaaaccctacttaggtcatcagggcaggagttctcactcccattttacagatga 2112 gaatactgaggcctggacaggtgaagtgaccagagagcaaaaggcaaaggggtgggggctgggtgcagtggctcac 2188 acctgtattcccaacacttttggaggctgaggttggaggattgcttgagcccaggaattcgagaccagcctaggtg 2264 acatagtgagaccccatctctacaaaaaataaaaaattaaccaggtgtggtggcacgtgcctgggagtcccagcga 2340 cttgggaggctgaggtgggaggattgtttgagcctgggaggtcgaggctgtagtgagccctgattgcaccactgta 2416 

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And Their Use, Especially for The Screening of Drugs

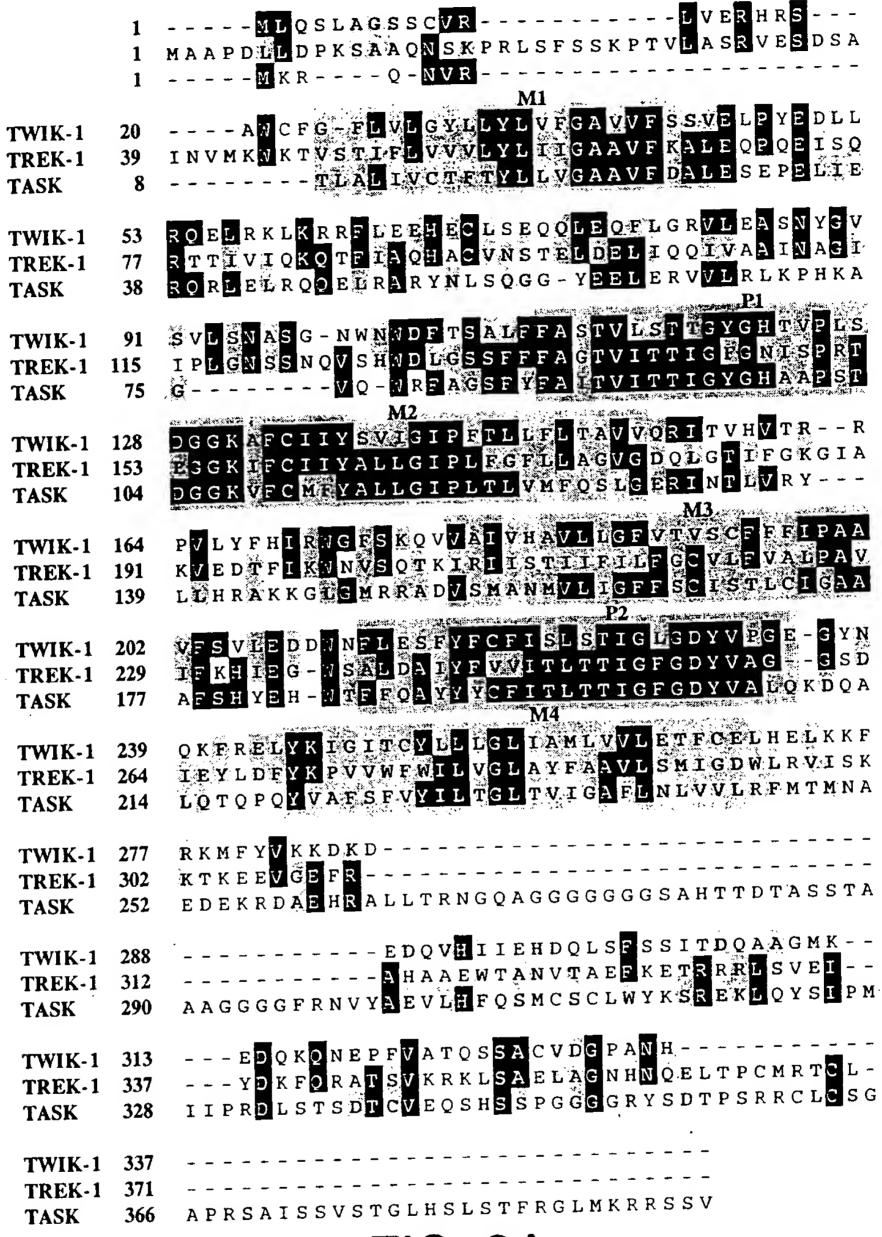
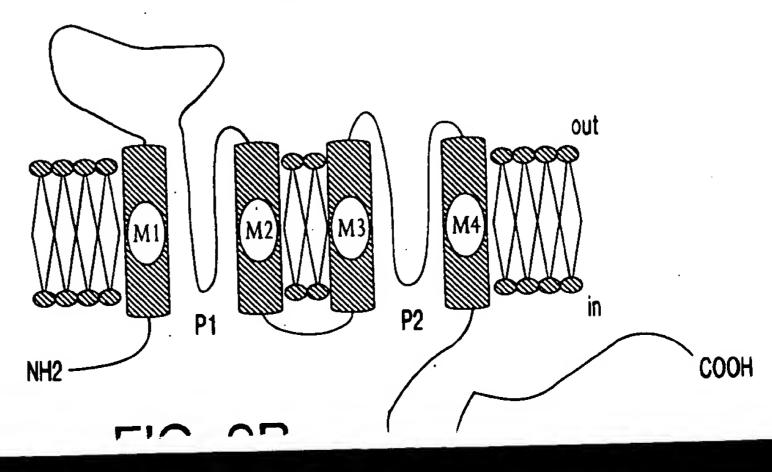


FIG. 9A



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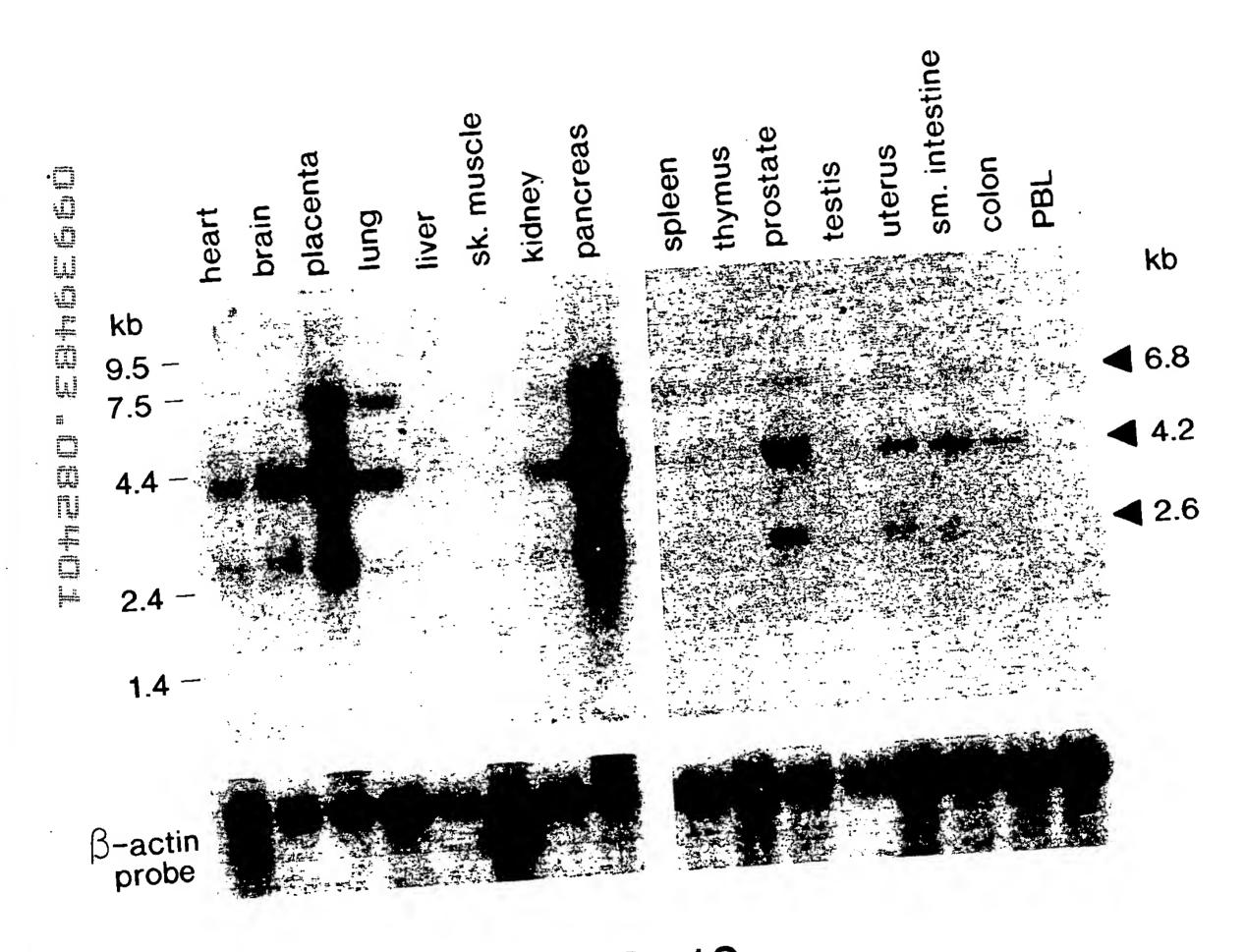


FIG. 10

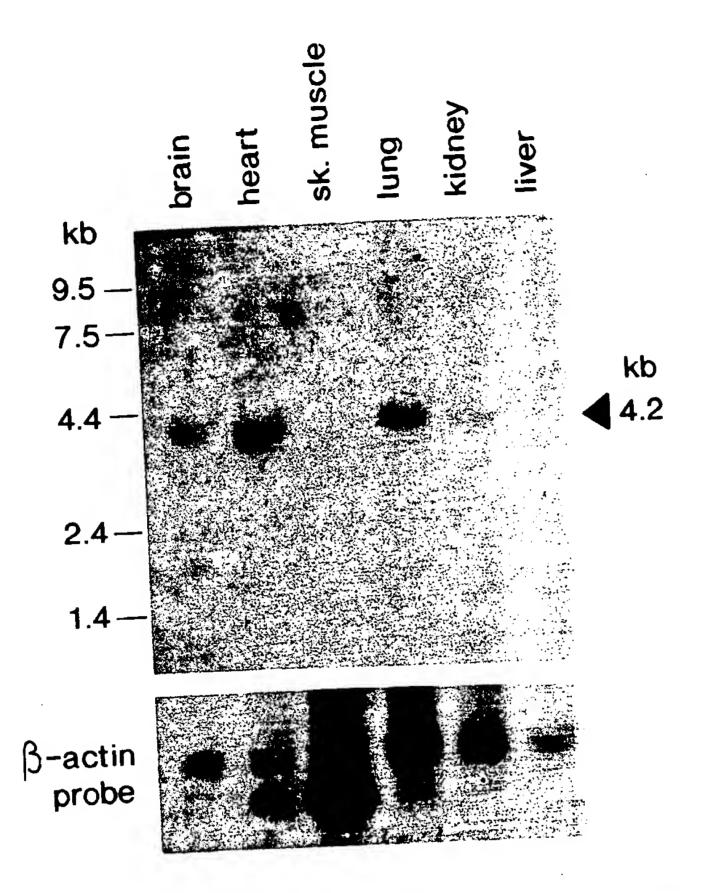


FIG. 11A

FIG. 11B

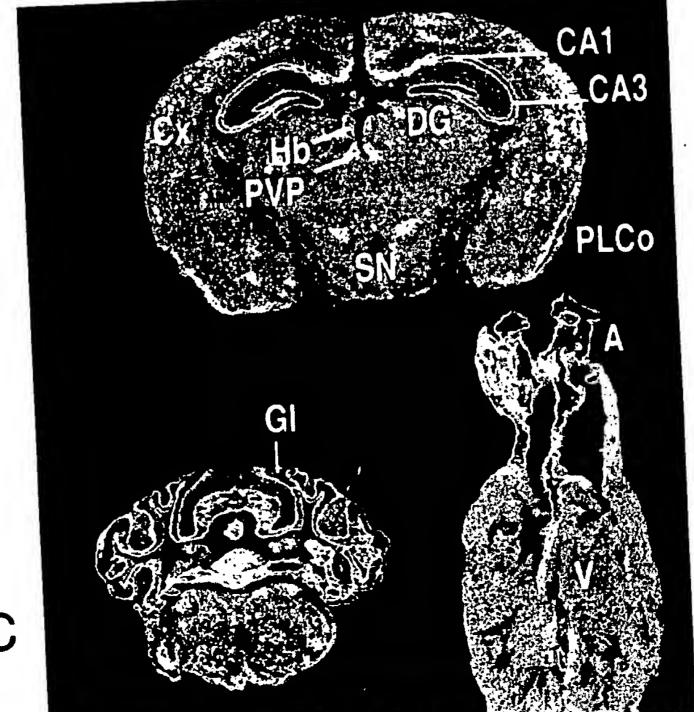


FIG. 11C

FIG. 11D

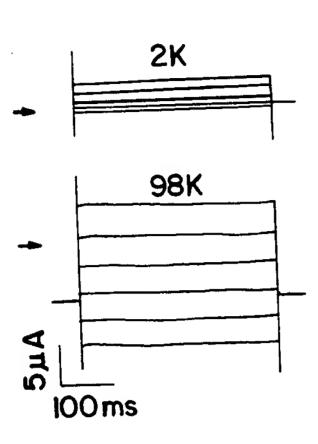
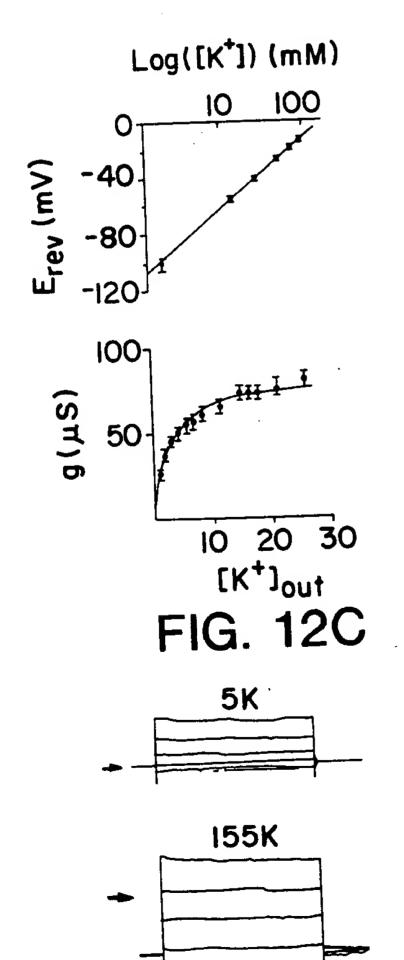


FIG. 12A



EIC . 10E

200 ms

2 nA

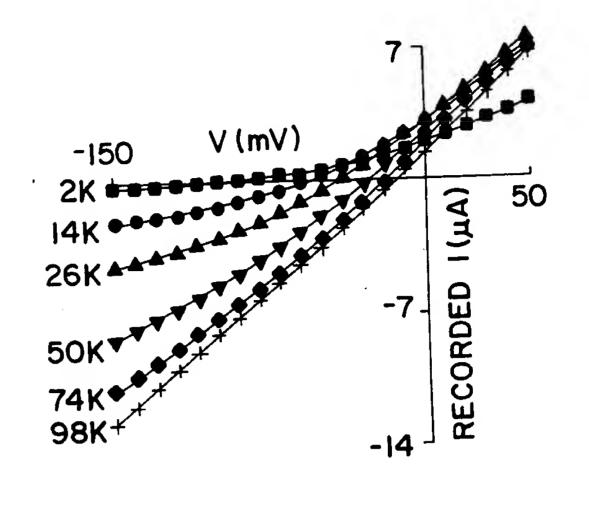


FIG. 12B

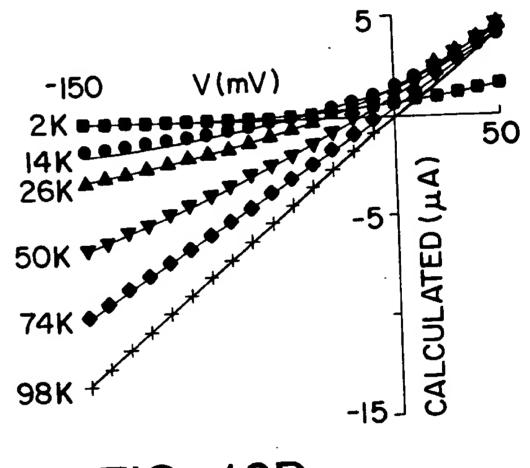


FIG. 12D

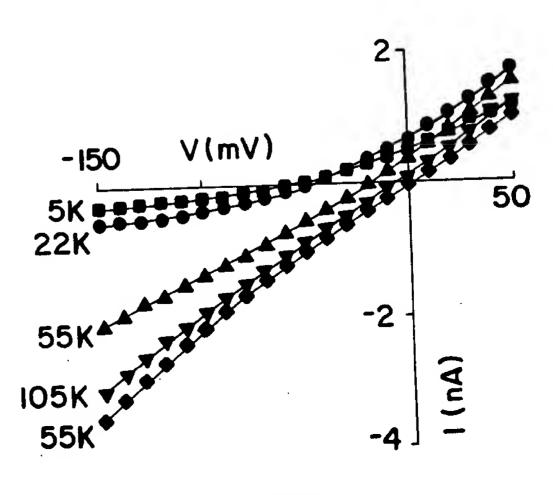


FIG. 12F

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The state and the state and

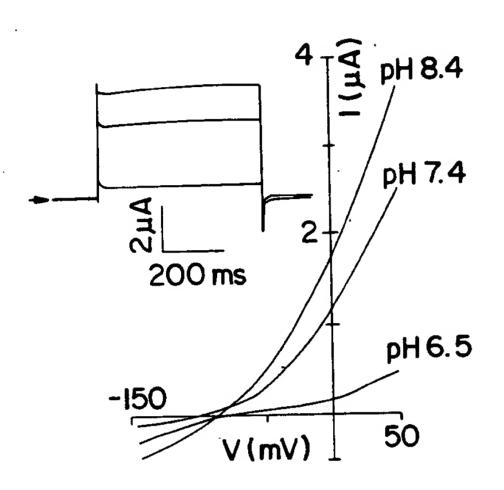


FIG. 13A

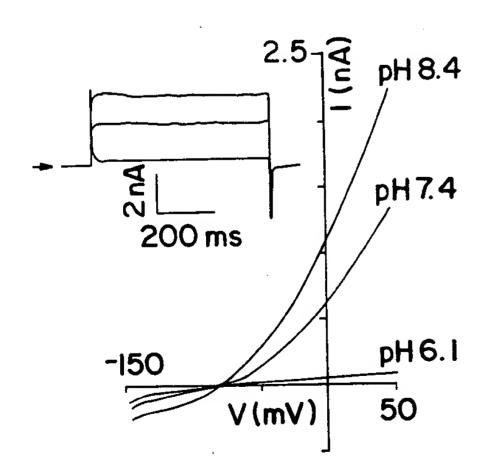


FIG. 13C

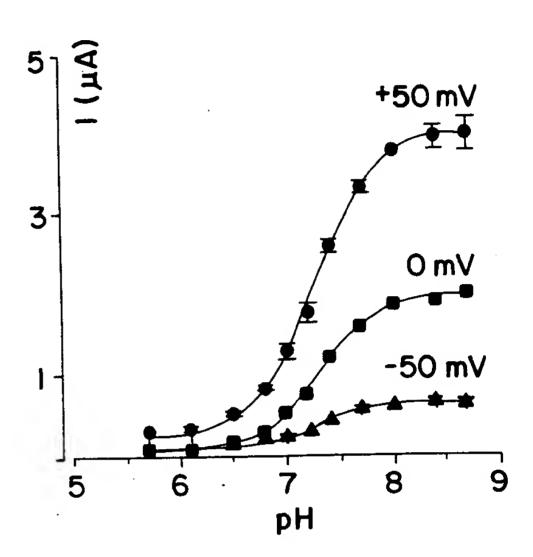


FIG. 13B

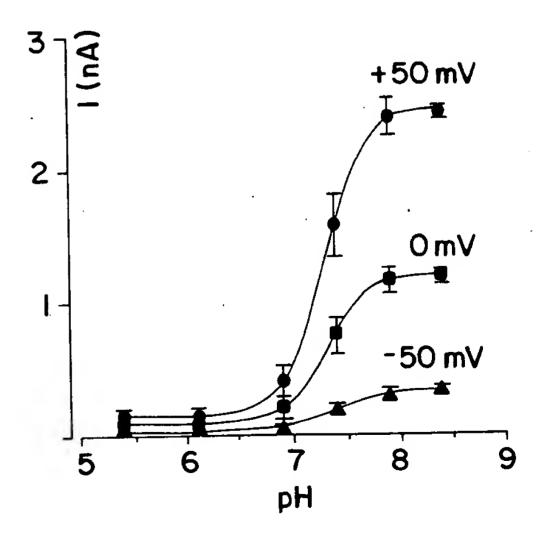


FIG. 13D